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**TITLE:** Associations between adolescent chronic pain and prescription opioid misuse in adulthood.

Cornelius B. Groenewald, MB,ChB\*, Emily F. Law, PhD\*, Emma Fisher, PhD‡, Sarah E. Beals-Erickson, PhD§, Tonya M. Palermo, PhD\*†¶

\*Departments of Anesthesiology and Pain Medicine, †Pediatrics, and ¶Psychiatry, University of Washington School of Medicine, Seattle, Washington

‡Department for Health, University of Bath, Claverton Down, Bath, BA27AY, UK.

§Children's Mercy Hospital and University of Missouri-Kansas City, Kansas City, Missouri; Division of Developmental and Behavioral Sciences

Corresponding Author:

Cornelius B. Groenewald, MB, ChB

Anesthesiology and Pain Medicine,

Seattle Children's Hospital,

M/S MB.11.500.3

4800 Sand Point Way NE,

E-mail: [Cornelius.groenewald@seattlechildrens.org](mailto:Cornelius.groenewald@seattlechildrens.org)

Seattle, WA 98105

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**Abstract**

Prescription opioid misuse is a serious public health concern, yet antecedent factors are poorly described. Using data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) (n = 14,784), we examined the longitudinal relationship between history of adolescent chronic pain and odds of misusing prescription opioids in adulthood. The primary predictor variable was chronic pain status during adolescence. The primary outcome variables were prescription opioid misuse during early adulthood and adulthood. Multivariate models controlled for known risk factors of opioid misuse, including sociodemographics (sex, race and ethnicity), adolescent mental health symptoms (anxiety, depression), adolescent self-reported physical health status, adolescent substance use/abuse, childhood trauma, and adult legitimate opioid use. We found that adults with a history of adolescent chronic pain were more likely to misuse opioids compared to those without history of chronic pain, even after controlling for other known risk factors. Further, we found that among individuals with history of adolescent chronic pain that race (white), other substance use, and exposure to trauma were risk factors for later opioid misuse. Longitudinal associations between adolescent chronic pain and subsequent adult prescription opioid misuse highlight the need for early targeted screening and prevention efforts that may reduce later opioid misuse.

**Perspective**

Using a large nationally representative sample, we found that chronic pain during adolescence was an independent risk factor for opioid misuse in adulthood, over and above other known risk factors. Furthermore, among those individuals with adolescent chronic pain, substance use, exposure to trauma, and race was associated with opioid misuse.

**Keywords**

Adolescent; chronic pain; opioid misuse

## Introduction

Prescription opioid misuse is defined as the consumption of opioids in manner or dose other than prescribed, consuming others' prescriptions, or consuming opioids for feelings that are elicited (i.e. to get high)<sup>31</sup>. Prescription opioid misuse is a serious public health epidemic in the United States. In 2013, almost 10 million Americans (4.9% of the adult population) reported prescription opioid misuse<sup>15</sup>. Prescription opioid misuse was found to be most prevalent among young adults 18-26 years of age, of whom 7.1% reported opioid misuse over the past 12 months in 2016 in the United States<sup>4</sup>. Cumulatively, by age 28, almost 23- 30% of Americans report misusing opioids at some point during their lifetime according to data from the National Longitudinal Study of Adolescent Health (Add Health; 2008) and National Survey on Drug Use and Health (2014)<sup>45, 3</sup>.

Prescription opioid misuse among young adults is associated with severe consequences including reduced employment<sup>1</sup>, sexual victimization<sup>19</sup>, and driving under the influence<sup>52</sup>. Furthermore, opioid misuse is a key antecedent for opioid use disorder, which may be characterized as a problematic pattern of opioid use that causes significant impairment or distress<sup>5</sup>. Indeed, opioids accounts for >50% of drug-related emergency department visits<sup>30</sup> and unintentional opioid overdose deaths now exceed those for all other illicit drugs in the USA<sup>40</sup>. In 2016, 2.1 million Americans reported having an opioid use disorder<sup>4</sup>.

Risk factors for opioid misuse remain poorly understood, yet many of the risk factors identified thus far are already present during adolescence including a history of substance abuse<sup>25</sup>, anxiety and depressive symptoms<sup>9</sup>, a history of childhood trauma<sup>37</sup>, higher socioeconomic status<sup>45</sup>, female sex<sup>28</sup>, and white, non-Hispanic race<sup>26</sup>. Better identification of

risk factors would allow targeted screening and prevention efforts during childhood, reducing the incidence and negative impact of later opioid misuse.

Chronic pain in adolescence is a potentially important individual difference factor that may help explain risk of prescription opioid misuse. Chronic pain affects 15-25% of adolescents<sup>21</sup> and adolescents with chronic pain share some similar characteristics to those who develop prescription opioid misuse, including an increased prevalence of exposure to childhood trauma<sup>16</sup> and increased rates of anxiety and depression<sup>32</sup>. Furthermore, a recent meta-analysis found that 25% of adults with chronic pain misuse prescription opioids<sup>50</sup>. However, studies have not yet identified whether having chronic pain during adolescence is associated with increased risk for future prescription opioid misuse in adulthood.

Thus, the primary aim of this study was to determine associations between adolescent chronic pain and subsequent prescription opioid misuse in adulthood in a large, nationally representative sample of individuals in the United States. We hypothesized that adults with a history of chronic pain during adolescence were more likely to misuse prescribed opioids, over and above other known risk factors of opioid misuse, including sociodemographic variables (sex, race, ethnicity, and income), adolescent mental health symptoms (anxiety and depressive), adolescent substance use/abuse, history of childhood trauma, and legitimate opioid use during adulthood. Our second aim was to explore specific risk factors associated with subsequent prescription opioid misuse in adulthood among individuals with a history of adolescent chronic pain. We hypothesized that the following risk factors in adolescence would predict increased risk for prescription opioid misuse in adulthood: higher household income, greater anxiety and depressive symptoms, greater substance use scores, and a larger number of traumatic experiences in childhood. Findings from these analyses will provide health care providers with a better understanding about which of their adolescent patients with chronic pain are at increased risk for future problematic opioid use.

## Methods

### Participants and procedure

For this cross-sectional analysis we used data from the National Longitudinal Study of Adolescent Health (Add Health)<sup>29</sup>. Add Health is a nationally representative, stratified, random sample of 20,745 United States participants starting in 1995 when participants were 11-21 years of age ( $M_{\text{age}} = 16$  years,  $S.D = 1.7$  years). Add Health combines longitudinal survey data on respondents' sociodemographic factors, physical and mental health, and substance use, providing unique opportunities to study how risk factors in adolescence are linked to health outcomes in adulthood.

Add Health uses a complex, multistage sample design and oversamples minorities. By applying survey weights, estimates are representative of the United States population. Thus far, participants have completed four subsequent waves of in-home interviews, the most recent of which was in 2008 when participants were between the ages of 24 and 34 years ( $M_{\text{age}} = 29$  years,  $S.D = 1.7$  years). Waves include: Wave I (adolescents 11–21 years of age, assessed in 1995); Wave II (adolescents 12-22 years of age, assessed in 1996); Wave III (early adulthood, 18–28 years of age, assessed in 2002); and Wave IV (adulthood, 24–34 years of age, assessed in 2008). We extracted data from all 4 Waves. The sample size included participants who completed all of the relevant items and waves ( $n = 14,784$ ). Participant characteristics are presented in Table 1. Additional information on Add Health is available at <http://www.cpc.unc.edu/projects/addhealth>. Add Health data are publically available and therefore the Institutional Review Board at Seattle Children's Hospital deemed this study exempt from review.

### Measures

Figure 1 outlines Add Health waves and measures assessed at each time point.

**Chronic pain.** Adolescents completed a general health survey during Waves I and II, which assessed pain location and frequency. Adolescents were asked to rate the frequency of common types of pain conditions over the previous 12 months (headache, stomachache, and aches, pain, or soreness in muscles or joints). Adolescents reported whether they experienced each pain “never,” “just a few times,” “about once a week,” “almost every day,” or “every day.” We dichotomized pain as “chronic” or “not chronic.” To avoid overinflating rates and keeping consistent with definitions of “high-frequency pain” used in previous literature, we used a conservative classification of chronic pain to include pain occurring “almost every day” or “every day,” consistent with previous publications using data from Add Health<sup>32, 47</sup>. Moreover, prevalence rates of chronic pain within this data set (21.9%) were similar to those cited in previous research<sup>21</sup>.

**Prescription opioid misuse.** Prescription opioid misuse was measured in the Waves following chronic pain measurement. Thus, while chronic pain was measured at Waves I and II, prescription opioid misuse was measured in Waves III and IV. Specifically, in the Add Health study, assessments were conducted to identify which participants initiated prescription opioid misuse between Waves II and III, and again between Waves III and IV. This design allowed us to determine which individuals had chronic pain in adolescence prior to reporting prescription opioid misuse in adulthood.

We used self-report data from Waves III and IV to measure cumulative prescription opioid misuse. The exact item stems varied slightly across Waves, reflecting different opioids available in the United States between Waves. Wave III prescription opioid misuse was identified by the following question: *“Since June 1995 (Wave II), have you taken any of the following drugs without a doctor’s permission: pain killers such as Darvon, Demerol, Percodan or Tylenol with codeine?”* with a binary response option of “yes” or “no”. Wave IV prescription opioid misuse was identified by the following question: *“Which of the following prescription drugs have you taken that were not prescribed for you, taken in larger amounts than prescribed,*

*for longer periods than prescribed, or that you only took for the feeling or experience they caused: pain killers or opioids such as Vicodin, OxyContin, Percocet, Demerol, Percodan or Tylenol with codeine not prescribed?”* with a binary response option of “yes” or “no”. For analyses, responses at each wave were coded as a binary variable, no opioid misuse = 0 and any opioid misuse = 1.

**Sociodemographics:** During Wave I adolescents reported their age, sex, race, and ethnicity. Parents reported their household income.

**Anxiety symptoms:** Adolescents completed a questionnaire assessing five physiological anxiety symptoms during Wave I. This approach has been used in previous Add Health studies<sup>18</sup> to assess anxiety symptoms. Specifically, adolescents were asked the frequency of each of the following symptoms over the past 12 months: (1) felt hot all over suddenly, for no reason; (2) cold sweats; (3) chest pains; (4) fearfulness; and (5) trouble relaxing. Responses to each item were measured using a 5-point Likert scale (anchors: 0 = “never”; 4 = “every day”). Similar to previously published research using this variable in the Add Health database, total anxiety symptom scores were calculated as a sum of the 5 items, with a possible range from 0 (no anxiety symptoms) to 20 (frequent/severe anxiety symptoms)<sup>18</sup>.

**Depressive symptoms:** Adolescents completed the 20-item Center for Epidemiologic Studies-Depression Scale (CES-D) at Wave I. Items were scored based on the frequency at which depressive symptoms were experienced in the past week using a 4-point Likert scale (anchors: “never/rarely” and “most/all of the time”). Similar to previously published Add Health studies, total scores were calculated as a sum of the 20 items and could range from 0 (no depressive symptoms) to 60 (frequent/severe depressive symptoms)<sup>41</sup>.

**General health:** Adolescents responded to the question *“In general, how is your health?”* with 5 response options ranging from “excellent” to “poor” in Wave I. For analyses, response options were dichotomized as either “good” (responses of “excellent,” “very good,” or



“good”) or “fair-poor” (responses of “fair” or “poor”). For analyses, the referent of “fair-poor” was coded as 0 and “good” was coded as 1.

**Other substance use in adolescence:** At Wave 2, adolescents responded to the following 6 items assessing other substance use behaviors: *“Have you”* (1) “ever regularly smoked one or more cigarettes per day”, (2) “had 5 or more drinks in a row over the past 12 months”, (3) “ever tried marijuana”, (4) “ever tried cocaine”, (5) “ever tried inhalants, such as glue”, and (6) “ever tried any other illegal drugs such as LSD, PCP, heroin, pills, etc”. Response options for all 6 items were binary (“yes” vs. “no”). Prior Add Health publications have used these items to characterize substance use behaviors during adolescence<sup>45</sup>. For analyses, we summed these six dichotomous variables (“yes” = 1, “no” = 0) to create a continuous variable representing 0-6 total substances used where higher scores indicate a greater number of substances used.

**Childhood trauma:** Using data from Waves I, III, and IV, adolescents responded to 9 items assessing exposure to childhood trauma. Specifically, adolescents were asked how often the following happened: (1) “being left alone when an adult should have been present >6 times”; (2) “not having adults taking care of their basic needs >6 times”; (3) “being slapped, kicked, or hit by an adult caregiver >6 times”; (4) “being touched in a sexual way or being forced to touch an adult in a sexual way”; (5) “having Social Services investigate or try to take them out of their living situation”; (6) “witnessed or threatened with physical violence”, (7) “someone stabbed you”, (8) “someone shot at you”; or (9) “someone physically assaulted/beaten you up”. Response options for all 9 items were binary (“yes” vs. “no”), Consistent with previously published Add Health studies<sup>13</sup>, we summed these nine dichotomous variables (“yes” = 1, “no” = 0) to create a continuous variable representing 0-9 total individual traumas experienced during childhood<sup>37</sup>.

**Legitimate opioid use during adulthood:** During Wave IV interviewers asked participants to provide information on all prescription medications consumed in the last four

weeks. These medications were categorized into therapeutic classes using the Multum Lexicon™ database. We identified all participants who reported taking a prescribed opioid.

### **Statistical analysis plan.**

All analyses were conducted using the survey package contained in Stata version 12.1 (StataCorp College Station, TX);  $\alpha$  was set at .05. We adjusted for the complex sample design of Add Health by using sampling weights, regional stratification, and primary sampling unit information to provide nationally representative estimates of the USA population.

To address aim one, we directly compared rates of prescription opioid misuse at both Wave III and Wave IV between adults who had chronic pain as adolescents to those who did not have chronic pain as adolescents. Next, we performed multivariate logistic regression analysis to determine the association between adolescent chronic pain status and adult prescription opioid misuse after controlling for other known risk factors including sociodemographic factors (sex, race and ethnicity, income), mental health (anxiety and depressive symptoms), physical health, other adolescent substance use/abuse, and exposure to childhood trauma. We also include legitimate opioid use during Wave IV as a co-variate in our model assessing associations between history of adolescent chronic pain and opioid misuse at Wave IV. However, we should note, that inclusion versus exclusion of this covariate did not affect the size or direction of our estimated odds ratios.

To address our second aim we used multivariate logistic regression analyses selecting only participants with history of chronic pain during adolescence to determine the association between hypothesized risk factors and subsequent prescription opioid misuse during adulthood among individuals with history of adolescent chronic pain. The dependent variable used in aim 2 was cumulative opioid misuse at Wave IV.

## **Results**

## **Sample description**

Our sample included 14,784 participants weighted to represent 21.93 million individuals nationally. Of these, 3,174 (weighted percentage: 21.9%) reported having chronic pain during adolescence. Sample characteristics, subdivided by chronic pain status, are presented in Table 1. Females reported chronic pain more frequently compared than males: while females represented 49.3% of the entire sample, they represented 57.4% of those with chronic pain. Adolescents with chronic pain, on average, reported higher depressive and anxious symptoms, and were more likely to rate their general health as fair or poor compared to adolescents without chronic pain. We also found that adolescents with chronic pain reported higher scores on both substance use and childhood trauma exposure variables compared to those without chronic pain.

### **Aim 1: Association between adolescent chronic pain history and prescription opioid misuse during early adulthood (Wave III) and adulthood (Wave IV).**

In the full sample, 19.9% of individuals reported initiation of prescription opioid misuse between Wave II (12-22 years of age; 1996) and Wave III (18-28 years of age; 2002; Table 1). Furthermore, an additional 8.4% of individuals reported initiation of prescription opioid misuse between Wave III and Wave IV (24-34 years of age; 2008). Thus, we found that by Wave IV, 3,248 participants (weighted percentage: 28.3%) endorsed prescription opioid misuse. The rate of reported prescription opioid misuse in early adulthood was higher among individuals with a history of reported adolescent chronic pain compared to those without chronic pain (24% versus 18.8%,  $p < 0.001$ ). Similarly, the rate of reported prescription opioid misuse in adulthood was also higher among individuals with a history of adolescent chronic pain versus those without (33% versus 27%,  $p < 0.001$ ). After controlling for multiple factors as specified in our logistic regression models, individuals with history of adolescent chronic pain had significantly increased odds of reported prescription opioid misuse in both early adulthood (adjusted odds ratio (AOR) = 1.24;

95% confidence interval (CI) 1.05-1.46,  $p = 0.013$ ; Table 2) and adulthood (AOR = 1.19; 95%CI: 1.04-1.36,  $p = 0.01$ ). We also found that younger participants were more likely to report opioid misuse compared to older participants, and that females were less likely to report opioid misuse. In addition black and Hispanic participants were less likely to report opioid misuse compared to white participants. Having a history of adolescent substance use and childhood trauma was associated with increased odds of reported opioid misuse. Legitimate opioid use in the preceding 4 weeks was associated with increased odds of opioid misuse. Self-reported depressive and anxiety symptoms and overall physical health reported as fair or poor were not associated with prescription opioid misuse.

## **Aim 2: Predictors of prescription opioid misuse within adults with a history of adolescent chronic pain.**

Table 3 presents results from our multivariate logistic regression analysis examining associations between adolescent risk factors and subsequent adult prescription opioid misuse among participants who had a history of adolescent chronic pain. Our findings partially supported our hypotheses. When investigating race, white adolescents were more likely to misuse opioids in adulthood than black adolescents (AOR = 0.40; 95%CI 0.23-0.69) and Hispanic adolescents (AOR = 0.42; 95% CI 0.25-0.71). Females were less likely to misuse opioids than males (AOR = 0.67; 95% CI 0.52-0.86). Contrary to our hypotheses, we did not find that higher depressive (AOR = 0.99; 95% CI 0.98-1.01) or anxiety symptoms (AOR = 1.02; 95% CI 0.96-1.08) were associated with prescription opioid misuse. However, higher scores on adolescent substance use (AOR = 1.27; 95% CI 1.17-1.39) and childhood trauma exposure (AOR = 1.38; 95% CI 1.21-1.58) were significantly associated with increased likelihood of misusing opioids in adulthood.

## **Discussion**

In this secondary analysis of an ongoing longitudinal survey we examined whether adolescent chronic pain increases risk for subsequent prescription opioid misuse in adulthood using a nationally representative sample of individuals in the United States. As we hypothesized, chronic pain status in adolescence was associated with an increased risk for prescription opioid misuse in early adulthood and adulthood over and above other known demographic and clinical covariates. Specifically, we found that the rate of opioid misuse in early adulthood was higher among individuals a history of adolescent chronic pain (24%) compared to those without a chronic pain history (19%). Similarly, the rate of opioid misuse in adulthood was higher among individuals with a history of adolescent chronic pain (33%) compared to those without a chronic pain history (27%). Our finding that 19.9% of 18-26 year olds misused opioids is similar to a previous report from the National Survey on Drug Use and Health, which found that 20.2% of 18-25 year old Americans had misused pain relievers in 2014<sup>3</sup>.

Among the sub-sample of individuals with a history of adolescent chronic pain, we also sought to identify risk factors for later prescription opioid misuse. Consistent with our hypothesis, we found that youth who were white, female, used other substances, and had a history of exposure to childhood trauma were particularly vulnerable to opioid misuse in adulthood. This pattern of results is generally consistent with prior research which has also found that opioid misuse is more likely among white children (as compared to racial and ethnic minority youth)<sup>26</sup>, youth who use marijuana or engage in binge drinking<sup>28</sup>, and youth with a history of physical abuse or assault<sup>37</sup>. Our finding that adolescent females may be at higher risk for later opioid misuse compared to males is somewhat difficult to interpret due to mixed findings in prior literature. For example, some epidemiologic studies have also identified a higher risk for opioid misuse among females<sup>43</sup>, while others have found females to be at either lower risk<sup>20</sup> or equivalent risk compared to males<sup>26</sup>. The etiology of the racial and ethnic differences in opioid misuse identified in our study and others is also poorly understood. For

example, a recent study examining racial and ethnic differences in opioid use between Mexican American adults vs. Non-Hispanic white and black American adults indicated that patient preferences and cultural values may influence differential rates of opioid use between racial and ethnic groups<sup>17</sup>. To our knowledge, similar research has not yet been conducted in pediatric populations.

Contrary to our hypothesis, symptoms of depression and anxiety among adolescents with chronic pain were not associated with later risk for opioid misuse. Psychological factors have been implicated in the persistence of chronic pain from adolescence to adulthood, including negative affect and pain catastrophizing<sup>51</sup>, yet the precise role of psychological functioning in the development of opioid misuse remains unclear. For example, Grattan et al. found that depression was associated with opioid misuse among adults with chronic pain<sup>12</sup>, while Hah et al. found that depression and anxiety were not associated with opioid misuse among adults with chronic pain in multivariate models<sup>14</sup>. On the other hand, Quinn et al. recently found strong associations between mental health diagnoses, including anxiety and depression, and long-term opioid use in adolescents although opioid misuse was not examined in that study<sup>38</sup>. Potential shared biological mechanisms between chronic pain and opioid use in childhood are also largely unexplored, although there has been some work in this area in animal models and adult populations that may be informative. In a recent review, Finan and colleagues (2017) proposed that chronic pain states may lead to changes in dopaminergic neurotransmission and mesolimbic system functions involved in the perception of pain, reward, and pain relief. Increased risk for problematic opioid use is proposed to result directly from these neurobiological changes, or may occur indirectly via changes in psychological functioning (i.e., increased negative affect, pain catastrophizing, pain-related fear)<sup>8</sup>. Limited available research suggests that, similar to their adult counterparts, youth with chronic pain also experience alterations in brain regions involved in pain processing, reward, and pain-related fear, with the amygdala being of particular importance<sup>44</sup>. Furthermore, both chronic pain and opioid misuse

are associated with genetic polymorphisms in dopaminergic pathways. For example, dopamine D2 receptors (DRD2)<sup>36</sup> and dopamine active transporters have been shown to alter pain perception and response to experimental pain in animal models and in adults with chronic pain conditions<sup>53</sup>. Dopamine has also been identified as an important contributor to the opioid reward system as evidenced by associations between opioid addiction and reduced expression of DRD2 receptors in the brain<sup>46, 11</sup>.

In addition to potential shared biological and psychological mechanisms, it is also important to consider social factors driving opioid use and the subsequent opioid epidemic in the United States. For example, recent nationwide increases in opioid prescribing to children and adolescents<sup>10</sup> may be attributed to the confluence of several societal changes including a growing understanding of pediatric pain<sup>21</sup> and its negative consequences<sup>39</sup>, increased vigilance towards pain management by regulatory agencies, and increased marketing of opioid medications to patients and providers by pharmaceutical companies. Treating pain with opioids is associated with increased risky opioid behaviors later in life<sup>2</sup>. For example Miech et al.<sup>28</sup> found that legitimate opioid use during adolescence was associated with a 33% increased risk for opioid misuse before age 23, while McCabe et al.<sup>24</sup> also found that that legitimate opioid use during adolescence was associated with opioid misuse at age 35. Next steps in this line of work should account for broader societal factors that may influence opioid prescribing practices and subsequent community-level and nationwide risk for opioid misuse and abuse across the lifespan. Our findings also suggest that a history of trauma and other substance use in adolescence may increase risk for opioid misuse later in life.

For youth with chronic pain conditions who may benefit from opioid medications, an important clinical consideration is ensuring adequate pain relief while minimizing risks of opioid misuse, overdose, and opioid use disorder. This is of particular importance for pediatric populations, as untreated or undertreated pain in childhood has the potential to substantially disrupt neurobiological<sup>42</sup> and psychosocial development<sup>34</sup>, and persist into adulthood<sup>51</sup>. It is

important to recognize that even for youth with chronic pain conditions who have a legitimate need for opioid medication, the gold standard for the management of pediatric chronic pain is interdisciplinary pain care, which may include pharmacotherapy but emphasizes the important role of behavioral pain management interventions, physical and occupational therapy, and complimentary and alternative modalities<sup>23</sup>. While we did not examine legitimate opioid use among adolescents in this study, our findings support the need for development of guidelines aimed at reducing risk for opioid misuse among children and adolescents with chronic pain.<sup>7</sup>

Consistent with prior research, our findings indicate that the majority of prescription opioid misuse was initiated between adolescence and early adulthood<sup>4</sup>. This suggests that adolescence may be a critical time for clinicians to identify risk for later opioid misuse and, potentially, to deploy preventive interventions directed at substance use behaviors. For example, adolescents often have unrestricted access to opioid medications at home<sup>27</sup>, and a recent survey found that 1 in 4 adolescents did not consider prescription opioid misuse to be a risky behavior<sup>35</sup>. Our findings support existing recommendations for health care providers, parents, and adolescents receiving an opioid prescription to receive education about: 1) the impact of prescription drug misuse on the developing brain; 2) safe storage and disposal of opioid medications in the home; and 3) prescription drug monitoring<sup>33</sup>. Our findings suggest that adolescents at increased risk for later opioid misuse (e.g., presence of chronic pain, other substance use, history of exposure to childhood trauma) may require closer monitoring to ensure appropriate use of opioid medications.

Findings from this secondary data analysis should be interpreted in the context of several limitations. First, chronic pain status in adulthood was not assessed in the Add Health survey; as a result, we cannot distinguish rates of opioid misuse between adults with vs. without concurrent chronic pain. Second, legitimate use of prescription opioids during adolescence was not assessed in the Add Health survey. Therefore, we are not able to determine rates of co-occurring opioid use and chronic pain in our sample prior to early adulthood and we are unable



to make conclusions about associations between opioid use and misuse in our sample. Third, opioid misuse was assessed using a single self-report item, and other factors related to patterns and drivers of opioid misuse were not assessed (e.g., frequency, motivation for misuse). As a result, we were not able to evaluate potentially relevant nuances such as differences by opioid type and the impact of motivation on the initiation of opioid use and misuse behaviors. To our knowledge, this limitation is not unique to our study as more comprehensive self-report measures of opioid misuse risk have not yet been validated for adolescent populations. Furthermore, existing measures developed for adult populations have demonstrated poor psychometric properties and limited clinical utility (see Voon, Karamouzian & Kerr, 2017 for a comprehensive listing)<sup>49, 6</sup>. Finally, different questions were used to assess opioid misuse in Wave III vs. Wave IV, which may have impacted our findings. Specifically, Wave IV asks about Oxycodone, Vicodin and Percocet, while Wave III also includes more detail on opioid misuse behaviors. The less comprehensive approach in Wave III may have led to underestimation of opioid misuse prevalence at that time point. Despite these limitations, the results from this study contribute to the limited evidence on the association between pediatric chronic pain and prescription opioid misuse.

In conclusion, this is the first nationally representative study to examine whether chronic pain in adolescence is associated with opioid misuse in adulthood. Chronic pain affects 15-25% of adolescents and is associated with increased risk for poor clinical outcomes in adulthood, including mental<sup>48</sup> and physical health symptoms<sup>51</sup> and alcohol and tobacco use<sup>22</sup>. Our study extends knowledge of the long-term outcomes associated with adolescent chronic pain by investigating subsequent prescription opioid misuse in adulthood. Our findings provide evidence that opioid misuse is more likely for adults with vs. without a history of adolescent chronic pain. This longitudinal association is of high public health importance, because the prescription opioid epidemic severely affects individuals in the United States across the lifespan. Early identification of at-risk individuals may minimize later prescription drug misuse. In our study, several risk

factors for opioid misuse later in life were identified including white race, female sex, other substance use, and history of childhood trauma.

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Figure 1. National Longitudinal Study of Adolescent to Adult Health (Add Health) waves and measures assessed at each wave.

Table 1. Wave I sociodemographic and baseline characteristics of individuals with and without history of adolescent chronic pain. Data source: Longitudinal study of adolescent to adult health.

Table 2. Multivariate logistic regression analyses testing the association between adolescent chronic pain history and prescription opioid misuse in adulthood at Wave III and Wave IV.

Table 3. Multivariate logistic regression analyses testing associations between hypothesized risk factors and prescription opioid misuse among participants with a history of chronic pain during adolescence.

Figure 1.

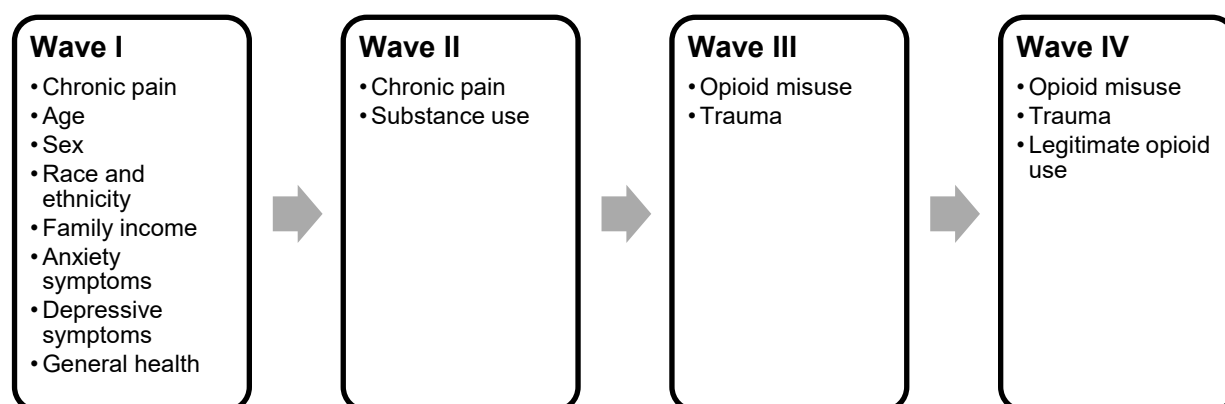


Table 1.

Characteristic	Full sample	No adolescent chronic pain	Adolescent chronic pain	<i>p</i>
Sample (n)	14784	11610	3174	
Estimated population (million)	21.9	17.1	4.8	
Mean age at Wave I (years)	16.0	16.0	16.0	0.94
Mean age at Wave IV (years)	28.9	28.9	28.9	0.76
Sex (female %)	49.3	47.1	57.4	<0.0001
Race and ethnicity (%)				0.25
White, non-Hispanic	65.6	65.2	67.5	
Black, non-Hispanic	15.5	15.5	15.5	
Hispanic	12.0	12.4	10.6	
Other	6.8	7.0	6.4	
Mean income (\$)	45665	46182	43994	0.11
Mean depressive symptoms (range 0-60)	11.4	10.4	14.9	<0.0001
Mean anxiety symptoms (range 0-20)	2.3	2.0	3.5	<0.0001
General health rated as fair-poor (%)	7.0	5.6	12.1	<0.0001
Substance use (range 0-6)	1.1	1.0	1.4	<0.0001
Childhood trauma exposures (range 0-9)	0.4	0.4	0.6	<0.0001
Legitimate opioid use during Wave IV (%)	5.2	4.7	6.9	<0.001
Prescription opioid misuse, Wave III (early adulthood) (%)	19.9	18.8	24.0	<0.0001
Prescription opioid misuse, Wave IV (adulthood) (%)	28.3	27.0	33.0	<0.0001



Table 2.

Characteristic	Early adulthood (Wave III)			Adulthood (Wave IV)		
	AOR	95% CI	p	AOR	95% CI	p
Adolescent chronic pain						
No	(ref)			(ref)		
Yes	1.24	1.05 -1.46	0.013	1.19	1.04 -1.36	0.013
Age	0.90	0.86 -0.95	<0.0001	0.88	0.85 -0.92	<0.0001
Sex						
Male	(ref)			(ref)		
Female	0.81	0.70 -0.94	0.006	0.76	0.66 -0.86	<0.0001
Race and ethnicity						
White, non-Hispanic	(ref)			(ref)		
Black, non-Hispanic	0.52	0.38 -0.72	<0.0001	0.39	0.29 -0.51	<0.0001
Hispanic	0.53	0.41 -0.69	<0.0001	0.50	0.40 -0.62	<0.0001
Other	0.87	0.65 -1.17	0.349	0.88	0.69 -1.13	0.311
Income	1.00	1.00 -1.00	0.092	1.00	1.00 -1.00	0.416
Depression	1.00	0.99 -1.01	0.911	1.00	0.99 -1.01	0.588
Anxiety	0.99	0.95 -1.03	0.704	0.99	0.95 -1.03	0.487
Health reported as fair-poor						
No	(ref)			(ref)		
Yes	0.96	0.71 -1.32	0.815	1.18	0.90 -1.56	0.223
Substance use	1.21	1.16 -1.27	<0.0001	1.27	1.22 -1.33	<0.0001
Childhood trauma exposures	1.32	1.23 -1.42	<0.0001	1.31	1.21 -1.41	<0.0001
Legitimate opioid use during Wave IV	-	-	-	1.95	1.53 -2.48	<0.0001

Table 3.

<b>Characteristic</b>	<b>AOR</b>	<b>95% CI</b>	<b>p</b>
Age	0.93	0.87 -1.00	0.065
Sex			
Male	(ref)		
Female	0.67	0.52 -0.86	0.002
Race and ethnicity			
White, non-Hispanic	(ref)		
Black, non-Hispanic	0.40	0.23 -0.69	0.001
Hispanic	0.42	0.25 -0.71	0.001
Other	1.40	0.86 -2.29	0.17
Income	1.00	1.00 -1.00	0.284
Depression	0.99	0.98 -1.01	0.473
Anxiety	1.02	0.96 -1.08	0.563
Health reported as fair-poor			
No	(ref)		
Yes	1.01	0.65 -1.57	0.967
Substance use	1.27	1.17 -1.39	<0.0001
Childhood trauma exposures	1.38	1.21 -1.58	<0.0001